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(56) Documents Cited

EP 0732079 A1 US 5125925 A

(58) Field of Search

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INT CL⁶ A61B , A61N 5/06
ONLINE:WPI

(54) Abstract Title

Photodynamic therapy of pituitary tumours

(57) A device for use in the photodynamic therapy of pituitary tumours, comprising a flexible catheter 1, an optical fibre 9 extending through the catheter 1 from a laser, the fibre 9 terminating at a position a small distance beyond the open end 3 of the catheter, a balloon 7 closing the said open end 3 of the catheter 1 and enclosing the end of the optical fibre 9, means 6 extending through the catheter 1 for supplying liquid for inflating the balloon 7, and at least one detector fibre 10 extending through the catheter 1 and emerging therefrom at a position spaced from the said end of the catheter 1 in such a manner as to rest against the external surface of the inflated balloon 7, the or each detector fibre 10 being connected to detector means arranged to control the quantity of energy delivered by the laser.

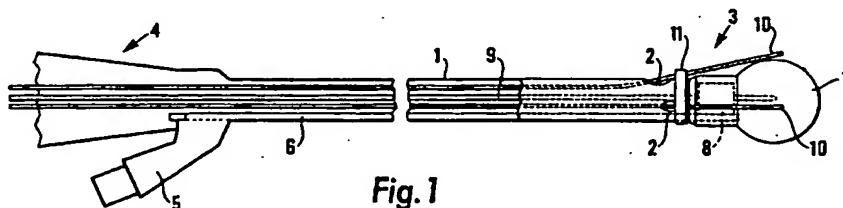


Fig. 1

At least one drawing originally filed was informal and the print reproduced here is taken from a later filed formal copy.

The claims were filed later than the filing date within the period prescribed by Rule 25(1) of the Patents Rules 1995

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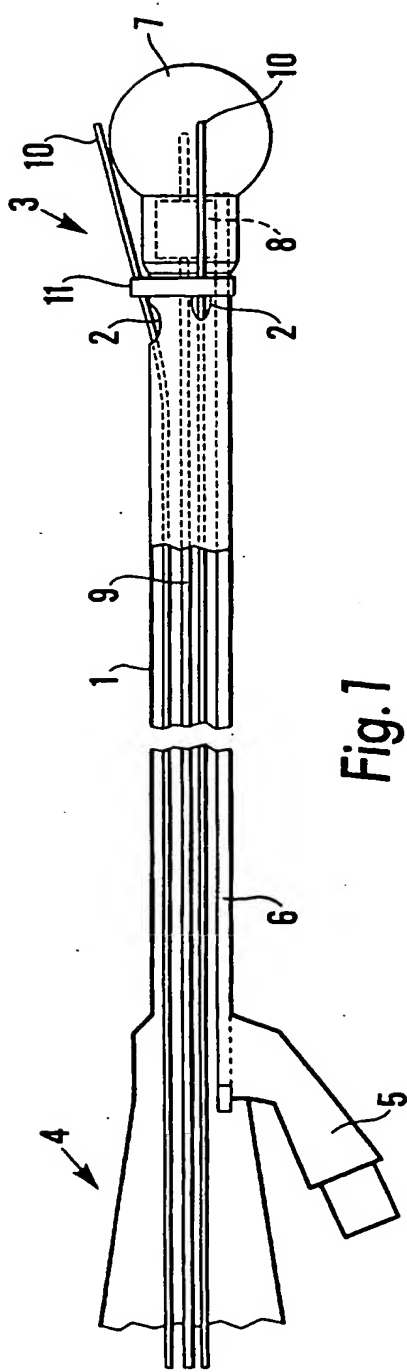


Fig. 1

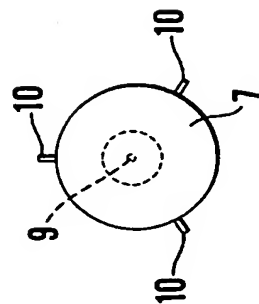


Fig. 2

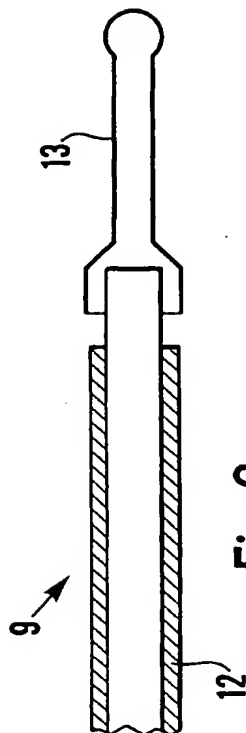


Fig. 3

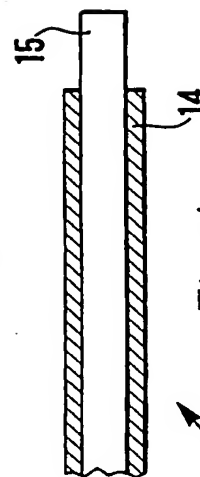


Fig. 4

DEVICE FOR PHOTODYNAMIC THERAPY OF PITUITARY TUMOURS

Field of the Invention

This invention relates to a device for use in the photodynamic therapy of pituitary tumours and the like.

Background to the Invention

Photodynamic therapy of brain tumours has been practised using an irradiator in which laser light from an optical fibre is diffused by means of a balloon inflated with, for example, a lipid solution. The balloon is mounted on the end of a tube of approximately 1.5 cm diameter, and is located in the cavity from which tumour tissue has been surgically removed, and inflated to a volume corresponding to that of the removed tissue. The optical fibre is then introduced into the balloon, and laser light is passed down the fibre for a time calculated according to the balloon volume and the output of the laser, determined by a power meter built in to the laser. The light output from the fibre is not directly measured prior to use, since this would compromise sterility, but it is checked immediately after the treatment by placing the end of the fibre into a calibrated integrating sphere photodetector, the resultant reading being used to determine the actual delivered light exposure.

This technique is not applicable to tumours of the pituitary gland, however, because it is insufficiently precise; damage to the surrounding brain tissue could prove fatal to the patient. The present invention seeks to provide a device which can be used safely and effectively in the photodynamic therapy of pituitary tumours.

Summary of the Invention

According to the invention, there is provided a device for use in the photodynamic therapy of pituitary tumours, comprising a flexible catheter, an optical fibre extending through the catheter from a laser, the fibre
5 terminating at a position a small distance beyond the open end of the catheter remote from the laser, a balloon closing the said open end of the catheter and enclosing the end of the optical fibre, means extending through the catheter for supplying liquid for inflating the balloon to a predetermined volume, and at least one detector fibre extending through the
10 catheter and emerging therefrom at a position spaced from the said end of the catheter in such a manner as to rest against the external surface of the inflated balloon, the or each detector fibre being connected to detector means arranged to control the quantity of energy delivered by the laser.

Preferably, three detector fibres are used, arranged so as to be equi-
15 spaced on the surface of the balloon. Means may be provided to hold the detector fibre or fibres in contact with the surface of the balloon, for example an elastic ring surrounding the catheter and the fibre or fibres adjacent to the said end.

The detector means may be arranged to control the length of operation of the laser, terminating its operation when the amount of light measured reaches a predetermined dose. Alternatively, the power of the laser
20 will be increased or decreased according to the intensity measured by the detectors, in order to give the required dose over a predetermined period.

The output of the three detector fibres may be averaged by the detector
25 means.

The liquid supplied to inflate the balloon is suitably a soybean oil emulsion, for example that available commercially under the Trade Mark INTRALIPID. A 0.25% concentration of the INTRALIPID material in water is sufficient.

- 5 A typical level of irradiation delivered by the device of the invention is 75 mWcm^{-2} for 1000 seconds, giving a dose of $75 \text{ Joules cm}^{-2}$ of energy. The laser is suitably an argon-dye laser generating red light at a wavelength of 630nm.

Brief Description of the Drawings

- 10 In the drawings, which illustrate an exemplary embodiment of the invention:

Figure 1 is a truncated longitudinal section of the device;

Figure 2 is an end view of the device showing the balloon inflated;

- Figure 3 is an enlarged view of the tip of the optical fibre delivering
15 the laser energy; and

Figure 4 is an enlarged view of the tip of one of the detector fibres.

Detailed Description of the Illustrated Embodiment

- Referring first to Figure 1, the device comprises a catheter 1 consisting of a flexible elongate tube formed from poly(vinyl chloride), open
20 at each end and with a series of three equi-spaced apertures 2 adjacent to the remote end 3 of the catheter which is inserted into the patient in use. At the other end 4 of the catheter, an inlet 5 is provided for introduction of liquid into a flexible pipe 6 which extends through the catheter and opens at the remote end 3 thereof.

The remote end 3 has a latex rubber balloon 7 fixed over it, and a seal 8 blocking it, the flexible pipe 6 passing through the seal 8 so as to be able to deliver liquid into the balloon to inflate it.

5 An optical fibre 9, described hereinafter in more detail with reference to Figure 3, passes through the length of the catheter 1 and through the seal 8, the free end of the fibre 9 being located at a position corresponding substantially to the centre of the balloon when inflated. At its other end, the fibre is coupled to an argon-dye laser (not shown).

10 Three additional optical fibres 10 also pass through the length of the catheter 1, emerging through respective ones of the three apertures 2 to rest against, and optically couple with, the surface of the inflated balloon 7 at three points equally spaced around its circumference. The three fibres 10 are connected at their other ends to a detector which can measure the average light output received by the three fibres 10 to monitor the
15 delivery of energy at the balloon's surface. An elastic ring 11 passes around the three fibres 10 after they have emerged from the catheter 1 to hold the fibres against the catheter, so that they press against the inflated surface of the balloon. Figure 2 illustrates the disposition of the ends of the fibres 10 around the surface of the inflated balloon 7.

20 Figure 3 illustrates the configuration of the end of the optical fibre 9 within the balloon. The fibre 9 is formed of glass, with a plastics sheath 12 over it. The sheath 12 is stripped away for a short distance at the end of the fibre, and a plastics diffusing tip 13 is fitted on to the stripped end by heat-shrinking. The tip 13 serves to spread the laser light, which is
25 then diffused further within the liquid in the balloon (0.25% INTRALIPID

soybean emulsion) so as to illuminate as evenly as possible the surface of the balloon 7.

Figure 4 shows the end of one of the detector fibres 10. The fibre 10 has a similar construction to the laser fibre 9, being plastics sheathed glass, but will typically be of smaller diameter than the laser fibre 9. The sheath 14 is stripped back from the glass fibre 15 for a short distance sufficient to allow the bare glass to rest of the surface of the inflated balloon 7 so that light within the balloon is coupled into the fibre for transmission back to the detector.

The device is employed in photodynamic therapy following surgery for the treatment of pituitary tumours. PHOTOFRIN (Trade Mark), a proprietary mixture of haemaporphyrins, is injected intravenously at a rate of 2mg kg^{-1} body weight 48 hours before transphenoidal hypophysectomy. The PHOTOFRIN material concentrates in tumour cells and is activated by exposure to light of the appropriate wavelength to produce tumour killing effects. Normal cells are protected from this effect because they do not normally concentrate the material.

Immediately following surgery, the tumour bed is illuminated by the device with 630nm laser light to activate the PHOTOFRIN material in the tumour cells, destroying them. The detector fibres 10 are forced into contact with the target tissue when the balloon is inflated by introduction of the INTRALIPID emulsion, allowing continuous monitoring of the intra-cavity fluence rate. The detector at the external end of the catheter receives the light conveyed by the detector fibres 10 and averages the three fibres' output to give a measure of the light being received by the tumour cells, altering the output of the laser to ensure that the precise

dose of energy is delivered to the target tissue. Typically, a dose of 75 Joules cm^{-2} is appropriate. Because of the precise control of the amount of light delivered to the cavity, the risk of damage to the sensitive surrounding tissue is minimised.

Claims

- 5 1. A device for use in the photodynamic therapy of pituitary tumours, comprising a flexible catheter, an optical fibre extending through the catheter from a laser, the fibre terminating at a position a small distance beyond the open end of the catheter remote from the laser, a balloon closing the said open end of the catheter and enclosing the end of the optical fibre, means extending through the catheter for supplying liquid for inflating the balloon to a predetermined volume, and at least
10 one detector fibre extending through the catheter and emerging therefrom at a position spaced from the said end of the catheter in such a manner as to rest against the external surface of the inflated balloon, the or each detector fibre being connected to detector means arranged to control the quantity of energy
15 delivered by the laser.
2. A device according to Claim 1, wherein three detector fibres are used, arranged so as to be equi-spaced on the surface of the balloon.
3. A device according to Claim 1 or 2, wherein means are provided
20 to hold the detector fibre or fibres in contact with the surface of the balloon.
4. A device according to Claim 3, wherein the said means comprises an elastic ring surrounding the catheter and the fibre or fibres adjacent to the said end.
- 25 5. A device according to any preceding claim, wherein the detector means are arranged to control the length of operation of the

laser, terminating its operation when the amount of light measured reaches a predetermined dose.

- 5 6. A device according to any of Claims 1 to 4, wherein the power of the laser is increased or decreased according to the intensity measured by the detectors, in order to give the required dose over a predetermined period.
7. A device according to Claim 6, wherein the output of the three detector fibres is averaged by the detector means.
8. A device according to any preceding claim, wherein the liquid
10 supplied to inflate the balloon is a soybean oil emulsion.
9. A device according to any preceding claim, wherein the laser is an argon-dye laser generating red light at a wavelength of 630nm.
10. A device for use in the phototherapy of pituitary tumours
15 substantially as described with reference to, or as shown in, the drawings.



The Patent Office

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Claims searched: 1-10

Examiner: Anwar Gilani
Date of search: 24 June 1998

Patents Act 1977 Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.P): A5R (REHR, RGAA)

Int Cl (Ed.6): A61N 5/06, A61B

Other: Online: WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
A	EP0732079 A1 (CORDIS EUROPA) col.1 1.3-15 and 26-30, col.2 1.48-col.3 1.12	1,6
A	US5125925 (LUNDAHL) whole document, particularly col.3 1.5-30, col.8 1.64-col.9 1.23, figures	1,6

X Document indicating lack of novelty or inventive step
Y Document indicating lack of inventive step if combined with one or more other documents of same category.
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P Document published on or after the declared priority date but before the filing date of this invention.
E Patent document published on or after, but with priority date earlier than, the filing date of this application.